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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,376	08/31/2000	Arun Kumar Sinha	U 012930	4436

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26 WEST 61ST STREET
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EXAMINER

KEYS, ROSALYND ANN

ART UNIT	PAPER NUMBER
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1621

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/652,376	Applicant(s) SINHA, ARUN KUMAR	
	Examiner Rosalynd Keys	Art Unit 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of Claims

1. Claims 1-7 are pending.
Claims 1-7 are rejected.
Claims 8-12 are cancelled.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 22, 2004 has been entered.

Claim Objections

3. Claim 4 is objected to because of the following informalities: the term "claamus" in line 2 is a misspelling of the term "calamus". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 1-7 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the reply filed June 22, 2004. In that paper, applicant has stated "The instant invention has successfully addressed a long-felt need to obtain economically viable product from the tetraploid and hexaploid strains of *Acorus calamus* and other plants." and "the instant invention does not merely lie in a hydrogenation reaction of a substituent group present on an aromatic compound. The instant invention uses hydrogenation to address a vital issue of great economic importance which is the high level toxicity of the β -asarone in the Asian varieties", these statements indicate that the invention is different from what is defined in the claim(s) because the claimed invention is directed to preparing 1-propyl-2,4,5-trimethoxybenzene of the formula I by steps (a)-(d), and not to reducing the toxicity of β -asarone in the hexaploid and tetraploid varieties of *Acorus calamus* as argued by Applicants in the remarks. Further in step (a) of claim 1, β -asarone does not even need to be present in the calamus oil undergoing reaction steps (b)-(d), since step (a) includes providing crude calamus oil, which given its broadest reasonable interpretation includes calamus oil with or without β -asarone. The Applicant admits on page 2 of the instant specification that it is known that the diploid plants do not contain the carcinogenic compound β -asarone. Thus, if Applicants invention is to reducing the toxicity of β -asarone in the Asian varieties the claims should be limited to such.

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Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Devgan et al. (Aust. J. Chem., 1968, 21, 3001-3003) alone or in view of Patra et al. (Journal of Natural Products, Vol. 44, No. 6, November-December 1981, pages 668 and 669) and further in view of March (Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, third edition, 1985, pp. 691-700 and 1093-1096) and Ma (US 3,757,490).

The instant claims are directed to a process for preparing 1-Propyl-2,4,5-trimethoxybenzene of the formula I comprising a) providing crude calamus oil or β -asarone in a solvent; b) hydrogenation of the solution in the presence of a catalyst at a pressure of 10-40 psi and a temperature in the range of 15-40°C; c) filtering the catalyst and removing the solvent under reduced pressure in the range of 10-100 mm Hg; and d) subjecting the reduced calamus oil to column of silica gel chromatography to obtain the desired product in liquid form with 85-97% purity. The calamus oil used can be of the tetraploid or hexaploid origin (see claim 3). The toxicity of the hydrogenated calamus oil can be two times less than the starting calamus oil (see claim 4). The

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reduced calamus oil can have a novel honey and roses aroma (see claim 5). The 1-Propyl-2,4,5-trimethoxybenzene obtained can have a novel sweet ylang, slightly spicy and fruity aroma (see claim 6). The calamus oil can be extracted from asarone rich plants (see claim 7).

Devgan et al. teach a) providing γ -asarone in alcohol; b) hydrogenating the solution in the presence of palladium-charcoal; c) filtering the catalyst off and removing the alcohol under suction; and the residue was chromatographed over neutral alumina and eluted with petroleum (see page 3003 under the title Dihydro- γ -asarone (II)). The product obtained was dihydro- γ -asarone, which corresponds to the compound having the formula I in claim 1.

The instant claims differ from Devgan et al. in that the instant invention employs β -asarone as the starting material instead of γ -asarone. However, β -asarone is an isomer of γ -asarone and is taught by Devgan et al. to have identical u.v. and i.r. spectra. One having ordinary skill in the art at the time the invention was made would have found it obvious to utilize the process of Devgan et al. to obtain the dihydro derivative of β -asarone, since β -asarone and γ -asarone are of such close structural similarity, further evidenced by their identical u.v. and i.r. spectra, that they would be expected to react similarly. This is further evidenced by the teachings of Patra et al., which shows that catalytic hydrogenation of β -asarone in the presence of 10% Pd/C in ethanol also gives the dihydroderivative of formula I (see entire disclosure in particular the paragraph above the acknowledgements on page 669). A long line of cases have held that the mere use of a different starting material, whether novel or known, in a conventional process to produce the product one would expect therefrom does not

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render the process unobvious. See for example *In re Surrey et al.* (CCPA 1963) 319 F2d 233, 138 USPQ 67; *In re Larsen* (CCPA 1961) 292 F2d 531, 130 USPQ 209; and *In re Durden, Jr. et al.* (CAFC 1985) 763 F2d 1406, 226 USPQ 359. The skilled artisan would have been further motivated to utilize the process of Devgan et al. because it allows the skilled artisan to isolate dihydro asarones, which are known to be useful for making antipsychotic agents.

The instant claims further differ from Devgan et al. in that Devgan fail to disclose a specific hydrogenation temperature and pressure, instead Devgan et al. teach that the hydrogenation practically stopped at 24°/706 mm).

March teaches that almost all known alkenes add hydrogen at temperatures between 0 and 275°C (see page 692). March teaches that many functional groups may be present in the molecule, e.g., OH, COOH, NH₂, CHO, COR, COOR, OR CN; and that although, some of these groups are also susceptible to catalytic hydrogenation, it is usually possible to find conditions under which double bonds can be reduced selectively (see page 692 and pages 1093-1096). β- and γ-asarone both contain the functional group COR. March teaches that hydrogenations in most cases are carried out at room temperature and just above atmospheric pressure, but some double bonds are more resistant and require higher temperatures and pressures (see page 693). March teaches that catalytic hydrogenation is the method most often used to reduce double bonds and that palladium-on-carbon is one of the most effective catalysts utilized (see pages 692 and 693). Both Devgan et al. and the applicants utilize Pd/C as a catalyst for conducting their hydrogenation processes. One having ordinary skill in the art at the time the invention was made would have found it obvious to utilize the

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conventional hydrogenation temperatures and pressures, as taught by March, to hydrogenate β -asarone to obtain its dihydro derivative, especially since a temperature and pressure within this range has already been shown to be effective on γ -asarone an isomer of β -asarone.

Devgan et al. fail to disclose the toxicity and aroma of the obtained hydrogenated asarone. However, one having ordinary skill in the art would expect the hydrogenated asarone to have the claimed characteristics since, a compound and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Devgan et al. fail to disclose the concentration of catalyst utilized. However, changes in temperature, concentrations, or other process conditions of an old process does not impart patentability unless the recited ranges are critical, i.e., they produce a new and unexpected result. *In re Aller et al.*, (CCPA 1955) 220 F.2d 454, 105 USPQ 233.

Devgan et al. fail to disclose the purity of the obtained dihydro asarone. However, when claiming a purer form of a known compound, it must be demonstrated that the purified material possess properties and utilities not possessed by the unpurified material. *Ex parte Reed*, 135 U.S.P.Q. 34, 36 (P.O.B.A. 1961), on reconsideration, *Ex parte Reed*, 135 U.S.P.Q. 105 (P.O.B.A. 1961).

Devgan et al. utilize a different adsorbent in step d). However, one having ordinary skill in the art would have found it obvious to utilize any adsorbent known for its use in chromatography in order to identify the product obtained (see column 3, lines 5-8 of the Ma patent, which teaches that alumina and silica gel are common adsorbents used in liquid-liquid and solid-liquid chromatography).

Response to Arguments

8. Applicant's arguments filed June 22, 2004 have been fully considered but they are not persuasive.

The Applicant argues that instant invention has successfully addressed a long-felt need to obtain economically viable product from the tetraploid and hexaploid strains of *Acorus calamus* and other plants. This argument is irrelevant since as stated above in the rejection of the claims under 35 USC 112, second paragraph, the instant invention is directed to a method of preparing 1-propyl-2,4,5-trimethoxybenzene of the formula I by steps (a)-(d) and not to reducing the toxicity of β -asarone in the tetraploid and hexaploid strains of *Acorus calamus*.

The Applicant argues that Devgan et al. dissuades a person skilled in art from reaching the conclusion that hydrogenating β -asarone will cause a reduction of toxicity. Therefore, Devgan et al. does not provide the required motivation to reduce toxicity in β -asarone by hydrogenation. This argument is irrelevant since as stated above in the rejection of the claims under 35 USC 112, second paragraph, the instant invention is directed to a method of preparing 1-propyl-2,4,5-trimethoxybenzene of the formula I by steps (a)-(d) and not to a method of hydrogenating β -asarone to cause a reduction in its toxicity.

With regard to the claimed invention, the Examiner believes that a prima facie case of obvious exists because the process taught by Devgan et al. for preparing the dihydro derivative of the formula I is identical to the instant process, except for its use of γ -asarone, which is an isomer of β -asarone. One having ordinary skill in the art would reasonably expect that the dihydro derivative of formula I could be isolated by utilizing

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the process of Devgan et al. on isomers of γ -asarone, especially since it already been demonstrated by Patra that one could successfully hydrogenate β -asarone to obtain the dihydro derivative of formula I.

Conclusion

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hoegberg et al. Journal of Medicinal Chemistry (1990), 33(4) CAPLUS abstract teaches the use of 1,2,4-trimethoxy-5-propyl benzene for preparing 3-substituted 5,6-dimethoxysalicylamides (I), which are useful as antipsychotic agents.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosalynd Keys whose telephone number is 571-272-0639. The examiner can normally be reached on M, R and F 3:30-8:30 pm and T-W 5:30-10:30 am.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Rosalyn Keys", is positioned above the printed name.

Rosalyn Keys
Primary Examiner
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August 19, 2004